

09/847,960

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Mar 5, 2004 (20040305/UP).

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(FILE 'HOME' ENTERED AT 07:45:15 ON 12 MAR 2004)

FILE 'STNGUIDE' ENTERED AT 07:45:34 ON 12 MAR 2004

FILE 'CAPLUS, EMBASE, BIOSIS, MEDLINE, WPIDS' ENTERED AT 07:45:46 ON 12 MAR 2004

L1 627 S (SWIFT, S? OR SWIFT S?)/AU,IN
L2 134 S (BOGENBERGER, J? OR BOGENBERGER J?)/AU,IN
L3 24 S L1 AND L2
L4 12 DUP REM L3 (12 DUPLICATES REMOVED)
L5 0 S (RIGEL) (2A) (PHARMAC?)
L6 5771 S (IG? OR IMMUNOGLOB? OR ANTIBOD?) (3A) (CLASS OR CLASSES OR ISOT
L7 1 S L6 AND (L1 OR L2)
L8 0 S (RNAASE) AND L6
L9 9 S (RNASE) AND L6
L10 5 DUP REM L9 (4 DUPLICATES REMOVED)
L11 56 S L6 AND ANTISENS?
L12 32 DUP REM L11 (24 DUPLICATES REMOVED)
L13 13430 S (RNA?) (3A) (PROTECT?) (3A) (ASSAY? OR PROBE? OR ENZYME?)
L14 0 S (L1 OR L2) AND L13
L15 0 S L13 AND L6
L16 930 S L13 AND (CANDIDATE? OR AGENT?)
L17 1 S L16 AND GERMLINE?
L18 402 S L16 AND TRANSCRIPT?
L19 165 S L18 AND (INHIBIT? OR MODULAT?)
L20 161 S L19 AND ASSAY?
L21 7 S L20 AND IGE
L22 3 DUP REM L21 (4 DUPLICATES REMOVED)
L23 32939 S (IG? OR IMMUNOGLOBULIN?) (3A) (EXPRESSION? OR TRANSCRIPT?)
L24 619 S L13 AND L23
L25 119 S L13 (10A) L23
L26 70 S L13 (5A) L23
L27 27 DUP REM L26 (43 DUPLICATES REMOVED)
L28 12432 S (IG OR IGE OR IMMUNOGLOBULIN?) (3A) (EXPRESSION? OR TRANSCRIPT?)
L29 32 S L28 AND L13
L30 14 DUP REM L29 (18 DUPLICATES REMOVED)
L31 257 S IG-I OR IG-II
L32 13 S L30 NOT L31

FILE 'STNGUIDE' ENTERED AT 08:14:13 ON 12 MAR 2004

FILE 'CAPLUS, EMBASE, BIOSIS, MEDLINE, WPIDS' ENTERED AT 08:15:21 ON 12 MAR 2004

FILE 'STNGUIDE' ENTERED AT 08:20:09 ON 12 MAR 2004

FILE 'CAPLUS, EMBASE, BIOSIS, MEDLINE, WPIDS' ENTERED AT 08:20:41 ON 12 MAR 2004

FILE 'STNGUIDE' ENTERED AT 08:21:19 ON 12 MAR 2004

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L32 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1989:210559 CAPLUS
DN 110:210559
TI Synthesis of germ-line $\gamma 1$ **immunoglobulin** heavy-chain
transcripts in resting B cells: induction by interleukin 4 and
inhibition by interferon γ
AU Berton, Michael T.; Uhr, Jonathan W.; Vitetta, Ellen S.
CS Southwest Med. Cent., Univ. Texas, Dallas, TX, 75235, USA
SO Proceedings of the National Academy of Sciences of the United States of
America (1989), 86(8), 2829-33
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB Interleukin 4 (IL-4) induces the **expression** of IgG1 and
IgE in lipopolysaccharide-stimulated B cells. Previous studies
have suggested that heavy-chain class switching may be regulated by
increasing the accessibility of specific switch regions to switch
recombinases. In this study, an **RNase protection**
assay was used to demonstrate that IL-4 induces expression of
germ-line $\gamma 1$ transcripts in B cells within 4 h of culture; induction
is dose-dependent and is inhibited by interferon γ . IL-4 alone is
capable of inducing the expression of germ-line $\gamma 1$ transcripts in
small, resting B cells, but lipopolysaccharide enhances expression. The
germ-line transcripts are the same size (1.8 and 3.4 kilobases) as the
secreted and membrane forms of the functional $\gamma 1$ mRNAs and
presumably result from the splicing of an upstream switch-region exon(s)
to the $\gamma 1$ constant-region exon(s). These data strongly support the
accessibility model for the regulation of isotype switching and suggest
that lymphokines such as IL-4 may direct specific switch events by
transcriptional activation of the corresponding switch regions.

L30 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6

AN 1989:210559 CAPLUS

DN 110:210559

TI Synthesis of germ-line $\gamma 1$ **immunoglobulin** heavy-chain
transcripts in resting B cells: induction by interleukin 4 and
inhibition by interferon γ

AU Berton, Michael T.; Uhr, Jonathan W.; Vitetta, Ellen S.

CS Southwest Med. Cent., Univ. Texas, Dallas, TX, 75235, USA

SO Proceedings of the National Academy of Sciences of the United States of
America (1989), 86(8), 2829-33

CODEN: PNASA6; ISSN: 0027-8424

DT Journal

LA English

AB Interleukin 4 (IL-4) induces the **expression** of IgG1 and
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increasing the accessibility of specific switch regions to switch
recombinases. In this study, an **RNase protection**
assay was used to demonstrate that IL-4 induces expression of
germ-line $\gamma 1$ transcripts in B cells within 4 h of culture; induction
is dose-dependent and is inhibited by interferon γ . IL-4 alone is
capable of inducing the expression of germ-line $\gamma 1$ transcripts in
small, resting B cells, but lipopolysaccharide enhances expression. The
germ-line transcripts are the same size (1.8 and 3.4 kilobases) as the
secreted and membrane forms of the functional $\gamma 1$ mRNAs and
presumably result from the splicing of an upstream switch-region exon(s)
to the $\gamma 1$ constant-region exon(s). These data strongly support the
accessibility model for the regulation of isotype switching and suggest
that lymphokines such as IL-4 may direct specific switch events by
transcriptional activation of the corresponding switch regions.

=>

L30 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 7
AN 1988:162606 CAPLUS
DN 108:162606
TI A homologous in vitro system to analyzed **transcription** of a
mouse **immunoglobulin** μ heavy-chain gene
AU Giller, Thomas; Brunner, Luzia; Pick, Leslie; Brack, Christine
CS Biozent., Univ. Basel, Basel, CH-4056, Switz.
SO European Journal of Biochemistry (1988), 172(3), 679-85
CODEN: EJBCAI; ISSN: 0014-2956
DT Journal
LA English

=> d 14 ab

L30 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 7
AB To investigate the mol. mechanisms of the regulation of **Ig** gene
transcription, a cell-free system was developed in which a cloned
mouse Ig μ heavy-chain gene was transcribed using nuclear exts. prepared
from a mouse B cell hybridoma line. To monitor transcription, an RNA-RNA
hybridization assay was developed in which a ^{32}P -labeled, SP6-synthesized
RNA probe complementary to Ig μ RNA was hybridized to unlabeled RNA
transcribed in the nuclear extract. Accurate initiation of transcription,
which resulted in the **protection** of the **RNA**
probe from digestion with nuclease S1, was detected by the separation
of the products on denaturing polyacrylamide gels, followed by autoradiog.
Using this assay, an in-vitro-synthesized RNA was detected. The 5' end of
the in-vitro-transcribed Ig μ RNA maps exactly to the same position as
the 5' end of the corresponding in vivo mRNA and its formation was
sensitive to the addition of low levels of α -amanitin (1 $\mu\text{g/mL}$),
indicating transcription by RNA polymerase II. It was shown by
competition expts. with oligonucleotides containing the decamer recognition
site that this sequence interacts with (a) decamer-binding factor(s) and
plays a pos. role in transcription. The competition effects of the
decamer-containing oligonucleotide appeared to be restricted to the decamer
motif present in the promoter region. No effects of the enhancer region
were detectable in vitro. Little or no transcriptional activity was found
in **transcription** expts. using the **Ig** μ promoter and
nuclear exts. prepared from HeLa cells. This suggests that tissue-specific
factors involved in Ig μ heavy-chain gene transcription are present in
the mouse B cell exts.

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L32-ANSWER 1 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:173821 CAPLUS

DN 138:220378

TI Gene Aiolos knock-out mouse as Systemic Lupus Erythematosus (SLE) model, cured in double Aiolos/OBF-1 knock out mice, and autoimmune disease drug screening methods

IN Matthias, Patrick Daniel; Sun, Jian

PA Novartis Forschungsstiftung, Zweigniederlassung Friedrich Miescher Institute for Biomedical Research, Switz.

SO PCT Int. Appl., 49 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003018836	A2	20030306	WO 2002-EP9365	20020821
	WO 2003018836	A3	20031030		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRAI GB 2001-20441 A 20010822

AB Homozygouse knock-out mice lacking the Aiolos gene are shown to exhibit multiple phenotypes in common with humans suffering from the autoimmune disease Systemic Lupus Erythematosus (SLE). When Aiolos -/- mice are crossed with homozygous knock out mice lacking the OBF-1 transcription factor gene, resultant double knock out mice lack all signs of SLE. Methods of screening for agents active against autoimmune diseases, for example SLE are provided. In vitro methods include screening for antagonists of OBF-1, screening for agents which inhibit binding of OBF-1 to oct-1 or oct-2, screening for agonists or antagonists of Aiolos protein and screening for agents which upregulate expression of Aiolos or down-regulate expression of OBF-1. Also disclosed are methods of screening using knock-out mice and B cells from knock-out mice.

L32-ANSWER 2 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:447458 CAPLUS

DN 135:194408

TI Liver-derived DEC205+B220+CD19- dendritic cells regulate T cell responses

AU Lu, Lina; Bonham, C. Andrew; Liang, Xiaoyan; Chen, Zongyou; Li, Wei; Wang, Liangfu; Watkins, Simon C.; Nalesnik, Michael A.; Schlissel, Mark S.; Demestris, Anthony J.; Fung, John J.; Qian, Shiguang

CS Thomas E. Starzl Transplantation Institute and Department of Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA, 15213, USA

SO Journal of Immunology (2001), 166(12), 7042-7052

CODEN: JOIMA3; ISSN: 0022-1767

PB American Association of Immunologists

DT Journal

LA English

AB Leukocytes resident in the liver may play a role in immune responses. We describe a cell population propagated from mouse liver nonparenchymal cells in IL-3 and anti-CD40 mAb that exhibits a distinct surface immunophenotype and function in directing differentiation of naive allogeneic T cells. After culture, such cells are DEC-205brightB220+CD11c-

CD19-, and neg. for T (CD3, CD4, CD8 α), NK (NK 1.1) cell markers, and myeloid Ags (CD11b, CD13, CD14). These liver-derived DEC205+B220+CD19- cells have a morphol. and migratory capacity similar to dendritic cells. Interestingly, they possess Ig gene rearrangements, but lack **Ig mol. expression** on the cell surface. They induce low thymidine uptake of allogeneic T cells in MLR due to extensive apoptosis of activated T cells. T cell proliferation is restored by addition of the common caspase inhibitor peptide, benzyloxycarbonyl-Val-Ala-Asp-fluoromethyl ketone (zVAD-fmk). T cells stimulated by liver-derived DEC205+B220+D19- cells release both IL-10 and IFN- γ , small amts. of TGF- β , and no IL-2 or IL-4, a cytokine profile resembling T regulatory type 1 cells. Expression of IL-10 and IFN- γ , but not bioactive IL-12 in liver DEC205+B220+CD19- cells was demonstrated by **RNase protection assay**. In vivo administration of liver DEC205+B220+CD19- cells significantly prolonged the survival of vascularized cardiac allografts in an alloantigen-specific manner.

RE.CNT 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:380823 CAPLUS
DN 135:15053
TI Differential gene expression in cancer
IN Kroes, Roger A.; Moskal, Joseph R.; Yamamoto, Hirotaka
PA Nyxis Neurotherapies, Inc., USA
SO PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001036685	A2	20010525	WO 2000-US31809	20001117
	WO 2001036685	A3	20020110		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
PRAI	US 1999-166056P	P	19991117		
	US 1999-166106P	P	19991117		
AB	The invention is directed towards methods for ascertaining gene expression characteristic for cancer, in particular brain cancers such as glioblastoma. A panel of 84 unique primer pairs were used to detect differentially expressed genes in tumorigenic glioma cell line (U373MG) by DDRT-PCR. At least 142 differentially expressed transcripts were found, in which 94 transcripts were appeared to be under-expressed while 48 transcripts were appeared to be over-expressed in the tumor cells. An addition 33 transcripts are differentially expressed in "old" and "young" tumors. Compns., methods and kits encompassing differential gene expression in cancer are provided.				

L32 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:125200 CAPLUS
DN 134:279548
TI Reduction in DNA binding activity of the transcription factor pax-5a in B lymphocytes of aged mice

AU Anspach, Jillian; Poulsen, Gail; Kaattari, Ilsa; Pollock, Roberta; Zwollo, Patty
 CS Department of Biology, The College of William and Mary, Williamsburg, VA, 23187, USA
 SO Journal of Immunology (2001), 166(4), 2617-2626
 CODEN: JOIMA3; ISSN: 0022-1767
 PB American Association of Immunologists
 DT Journal
 LA English
 AB Aging has been associated with intrinsic changes of the humoral immune response, which may lead to an increased occurrence of autoimmune disorders and pathogenic susceptibility. The transcription factor Pax-5 is a key regulator of B cell development. Pax-5a/B cell-specific activator protein and an alternatively spliced isoform, Pax-5d, may have opposing functions in transcriptional regulation due to the lack of a transactivation domain in Pax-5d. To study B cell-specific changes that occur during the aging process, the authors investigated expression patterns of Pax-5a and 5d in mature B cells of young and aged mice. **RNase protection assays** showed a similar transcriptional pattern for both age groups that indicates that aging has no affect on transcription initiation or alternative splicing for either isoform. In contrast, a significant reduction in the DNA binding activity of Pax-5a but not Pax-5d protein was observed in aged B cells in vitro, while Western blot analyses showed that similar levels of Pax-5a and 5d proteins were present in both age groups. The observed decrease in Pax-5a binding activity correlated with changes in expression of two Pax-5 target genes in aged B cells. **Expression** of the **Ig J** chain and the secreted form of **Ig μ** , which are both known to be suppressed by Pax-5a in mature B cells, were increased in B cells of aged mice. Together, these studies suggest that changes associated with the aging phenotype cause post-translational modification(s) of Pax-5a but not Pax-5d, which may lead to an abnormal B cell phenotype in aged mice, associated with elevated levels of J chain, and secretion of **IgM**.

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2000:550749 CAPLUS
 DN 134:54648
 TI Widespread B29 (CD79b) gene defects and loss of expression in chronic lymphocytic leukemia
 AU Thompson, Alexis A.; Do, Ha Nancy; Saxon, Andrew; Wall, Randolph
 CS Dept. of Pediatrics, Division of Hematology/Oncology, Gwynne Hazen Cherry Memorial Laboratories, UCLA, Los Angeles, CA, 90095, USA
 SO Leukemia & Lymphoma (1999), 32(5/6), 561-569
 CODEN: LELYEA; ISSN: 1042-8194
 PB Harwood Academic Publishers
 DT Journal
 LA English
 AB Chronic lymphocytic leukemia (CLL) is the most prevalent form of leukemia in Western countries, and is characterized by a monoclonal proliferation of primarily immature CD5+ B lymphocytes. The mol. biol. of chronic leukemias and lymphomas remains largely unresolved. Surface **Ig expression**, which is often decreased in CLL, requires the protein product of the B29 gene for translocation of the B cell antigen receptor complex (BCR) to the cell surface and for signal transduction. Because B29 is essential for intracellular assembly and transport of the B cell antigen receptor complex to the cell surface, the authors postulate that a perturbation in B29 could result in the diminished expression and function of surface Ig in leukemic CLL cells. The authors have found recurrent aberrations affecting the B29 gene in CLL cells. Analyses of 27 unselected cases of CLL demonstrate that over 75% had low to absent B29

expression which correlated directly to their level of surface **Ig expression**. Half of these surface B29low/- cases had either no or barely detectable levels of B29 mRNA by **RNAse protection assay**. To date, all of the CLL samples with normal B29 mRNA levels were found to have mutations or truncations which would significantly effect the structure and/or function of B29 protein. Strategies directed at correcting these B29 mutations are expected to induce increased lg surface expression in CLL and may improve the sensitivity of CLL cells to conventional cytotoxic chemotherapy.

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:722007 CAPLUS

DN 123:336954

TI Alternative splicing of CD79a (Ig- α /mb-1) and CD79b (**Ig**
- β /B29) RNA **transcripts** in human B cells

AU Hashimoto, Shiori; Chiorazzi, Nicholas; Gregersen, Peter K.

CS Departments Medicine, North Shore University Hospital and Cornell
University Medical College, Manhasset, NY, 11030, USA

SO Molecular Immunology (1995), 32(9), 651-9
CODEN: MOIMD5; ISSN: 0161-5890

PB Elsevier

DT Journal

LA English

AB The CD79a (Ig- α /mb-1) and CD79b (Ig- β /B29) mols. form a
membrane heterodimer that is non-covalently associated with surface membrane
Ig and is the major signaling component of the B cell antigen receptor
complex. We have defined variant RNA **transcripts** for both CD79a
(**Ig**- α /mb-1) and CD79b (Ig- β /B29) which appear to
arise by alternative splicing. These splice variants are predicted to
encode truncated forms of these mols. that result in the deletion of the
entire extracellular Ig-like domain of CD79b and of a major portion of the
extracellular domain of CD79a. The presence of these short transcripts in
a variety of human B cells and B cell lines was established by an
RNAse protection assay. The definition of
these variant transcripts provides a basis for a continuing effort to
define variant protein products of CD79a and CD79b and examine their role
in B cell physiol.

L32 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:558440 CAPLUS

DN 123:25860

TI **IgE**-dependent **expression** of interleukin-5 mRNA and
protein in human lung: modulation by dexamethasone

AU Glaum, Mark C.; Jaffe, Jonathan S.; Gillespie, David H.; Raible, Donald
G.; Post, Thomas J.; Wang, Yihe; Dimitry, Edward; Schulman, Edward S.

CS Department of Medicine, Hahnemann University, Philadelphia, PA, 19102, USA

SO Clinical Immunology and Immunopathology (1995), 75(2), 171-8
CODEN: CLIIAT; ISSN: 0090-1229

DT Journal

LA English

AB MRNA and protein expression of the Th2 cytokines IL-4 and IL-5 from human
lung were examined during the first 4 h following IgE-mediated triggering, a
time representative of the evolving late-phase reaction (LPR). Lung
explants were incubated for 16 h at 37° in culture media alone or
with added dexamethasone (10⁻⁶ M), washed, and then challenged with buffer
or anti-IgE (3 μ g/mL). Using **RNAse protection**
assays, in 16/16 individual lungs IL-5 mRNA expression was observed
at 4 h following anti-IgE and at no points following buffer challenge.
Fragments released 1129 ng of IL-5/g wet weight over a 24-h period. Neither
IL-4 transcripts nor protein were detected in any anti-IgE challenges.

Both the IgE-mediated IL-5 mRNA and protein responses were below the limits of detection following dexamethasone preincubation, suggesting a mechanism for the potent inhibitory effects of these agents observed in the LPR.

L32 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1994:628634 CAPLUS

DN 121:228634

TI T cell clones from an X-linked hyper IgM patient induce IgE synthesis in vitro despite expression of nonfunctional CD40 ligand

AU Life, Paul; Gauchat, Jean-Francois; Schnuriger, Valerie; Estoppey, Sandrine; Mazzei, Gonzalo; Durandy, Anne; Fischer, Alain; Bonnefoy, Jean-Yves

CS Glaxo Inst. Mol. Biol., Geneva, Switz.

SO Journal of Experimental Medicine (1994), 180(5), 1775-84
CODEN: JEMEAV; ISSN: 0022-1007

DT Journal

LA English

AB The induction of IgE switching in B cells requires at least 2 signals. The first is given by either of the soluble lymphokines interleukin 4 (IL-4) or IL-13, whereas the second is contact dependent. It has been widely reported that a second signal can be provided by the CD40 ligand (CD40L) expressed on the surface of T cells, mast cells, and basophils. A defect on the CD40L has been shown recently to be responsible for the lack of IgE, IgA, and IgG, characteristic of the childhood X-linked immunodeficiency, hyper IgM syndrome (HIGM1). IgE can however be detected in the serum of some HIGM1 patients. Here, the authors isolated T cell clones and lines using phytohemagglutinin (PHA) and allergen, resp., from the peripheral blood of one such patient who expressed a truncated form of CD40L, and investigated their ability to induce IgE switching in highly purified, normal tonsillar B cells in vitro. Unexpectedly, 4 of 12 PHA clones tested induced contact-dependent IgE synthesis in the presence of exogenous IL-4. These clones were also shown to strongly upregulate IL-4-induced germline κ RNA and formed dense aggregates with B cells. Of the 4 helper clones, 3 were CD8+, of which 2 were characteristic of the T helper cell 2 (Th2) subtype. Two allergen-specific HIGM1 T cell lines, both of the Th0 subtype, could also drive IgE synthesis when prestimulated using specific allergen. All clones and lines were neg. for surface expression of CD40L, and the mutated form of CD40L was confirmed for a representative clone by **RNase protection assay** and sequencing. The IgE helper activity could not be attributed to membrane tumor necrosis factor α (TNF- α) although it was strongly expressed on activated clones, and the addition of neutralizing anti-TNF- α antibody did not abrogate IgE synthesis. These results suggest the involvement of T cell surface mols. other than CD40L in the induction of IgE synthesis, and these mols. may also be implicated in other aspects of T-B cell interactions.

L32 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1993:426277 CAPLUS

DN 119:26277

TI Interferon- γ induces polymeric immunoglobulin receptor mRNA in human intestinal epithelial cells by a protein synthesis dependent mechanism

AU Piskurich, Janet F.; France, John A.; Tamer, Carol M.; Willmer, Carolyn A.; Kaetzel, Charlotte S.; Kaetzel, David M.

CS Inst. Pathol., Case West. Reserve Univ., Cleveland, OH, 44106, USA

SO Molecular Immunology (1993), 30(4), 413-21
CODEN: MOIMD5; ISSN: 0161-5890

DT Journal

LA English

AB Transport of secretory IgA into external fluids is mediated by the

polymeric Ig receptor (pIgR) on the surface of mucosal epithelial cells. The mechanism was studied by which interferon- γ (IFN- γ) induces pIgR expression in HT-29.74 cells, a subclone of the HT-29 cell line selected for high concns of pIgR. Here is reported the isolation of genomic DNA and cDNA clones encoding human pIgR and development of a sensitive **RNase protection assay** for pIgR mRNA. This assay was used to determine if induction of pIgR by IFN- γ is mediated by accumulation of pIgR mRNA. After an initial lag of 12 h, pIgR mRNA increased 7-fold in response to IFN- γ , reaching a plateau at 24 h. Concns. of pIgR protein also increased 7-fold, but the increase was delayed until 48 h following stimulation with IFN- γ . Cycloheximide treatment abolished the IFN- γ induced increase in pIgR mRNA, indicating that induction of pIgR mRNA by IFN- γ requires de novo protein synthesis. Apparently, the induction of pIgR expression by IFN- γ involves an increase in steady-state concns of pIgR mRNA via a protein synthesis dependent mechanism.

L32 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1989:210559 CAPLUS

DN 110:210559

TI Synthesis of germ-line γ 1 **immunoglobulin** heavy-chain **transcripts** in resting B cells: induction by interleukin 4 and inhibition by interferon γ

AU Berton, Michael T.; Uhr, Jonathan W.; Vitetta, Ellen S.

CS Southwest Med. Cent., Univ. Texas, Dallas, TX, 75235, USA

SO Proceedings of the National Academy of Sciences of the United States of America (1989), 86(8), 2829-33
CODEN: PNASA6; ISSN: 0027-8424

DT Journal

LA English

AB Interleukin 4 (IL-4) induces the **expression** of IgG1 and **IgE** in lipopolysaccharide-stimulated B cells. Previous studies have suggested that heavy-chain class switching may be regulated by increasing the accessibility of specific switch regions to switch recombinases. In this study, an **RNase protection assay** was used to demonstrate that IL-4 induces expression of germ-line γ 1 transcripts in B cells within 4 h of culture; induction is dose-dependent and is inhibited by interferon γ . IL-4 alone is capable of inducing the expression of germ-line γ 1 transcripts in small, resting B cells, but lipopolysaccharide enhances expression. The germ-line transcripts are the same size (1.8 and 3.4 kilobases) as the secreted and membrane forms of the functional γ 1 mRNAs and presumably result from the splicing of an upstream switch-region exon(s) to the γ 1 constant-region exon(s). These data strongly support the accessibility model for the regulation of isotype switching and suggest that lymphokines such as IL-4 may direct specific switch events by transcriptional activation of the corresponding switch regions.

L32 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1988:162606 CAPLUS

DN 108:162606

TI A homologous in vitro system to analyze **transcription** of a mouse **immunoglobulin** μ heavy-chain gene

AU Giller, Thomas; Brunner, Luzia; Pick, Leslie; Brack, Christine

CS Biozent., Univ. Basel, Basel, CH-4056, Switz.

SO European Journal of Biochemistry (1988), 172(3), 679-85
CODEN: EJBICAI; ISSN: 0014-2956

DT Journal

LA English

AB To investigate the mol. mechanisms of the regulation of **Ig** gene **transcription**, a cell-free system was developed in which a cloned mouse Ig μ heavy-chain gene was transcribed using nuclear exts. prepared

from a mouse B cell hybridoma line. To monitor transcription, an RNA-RNA hybridization assay was developed in which a ³²P-labeled, SP6-synthesized RNA probe complementary to Ig μ RNA was hybridized to unlabeled RNA transcribed in the nuclear extract. Accurate initiation of transcription, which resulted in the **protection** of the **RNA probe** from digestion with nuclease S1, was detected by the separation of the products on denaturing polyacrylamide gels, followed by autoradiog. Using this assay, an in-vitro-synthesized RNA was detected. The 5' end of the in-vitro-transcribed Ig μ RNA maps exactly to the same position as the 5' end of the corresponding in vivo mRNA and its formation was sensitive to the addition of low levels of α -amanitin (1 μ g/mL), indicating transcription by RNA polymerase II. It was shown by competition expts. with oligonucleotides containing the decamer recognition site that this sequence interacts with (a) decamer-binding factor(s) and plays a pos. role in transcription. The competition effects of the decamer-containing oligonucleotide appeared to be restricted to the decamer motif present in the promoter region. No effects of the enhancer region were detectable in vitro. Little or no transcriptional activity was found in **transcription** expts. using the Ig μ promoter and nuclear exts. prepared from HeLa cells. This suggests that tissue-specific factors involved in Ig μ heavy-chain gene transcription are present in the mouse B cell exts.

L32 ANSWER 12 OF 13 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 AN 2004:123346 BIOSIS
 DN PREV200400124354
 TI Nuclear factor-kappaB contributes to interleukin-4- and interferon-dependent polymeric **immunoglobulin** receptor **expression** in human intestinal epithelial cells.
 AU Ackermann, Laynez W.; Denning, Gerene M. [Reprint Author]
 CS VA Medical Center, 601 Highway 6 West, Building 3, Room 158, Iowa City, IA, 52246, USA
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 SO Immunology, (January 2004) Vol. 111, No. 1, pp. 75-85. print.
 CODEN: IMMUAM. ISSN: 0019-2805.
 DT Article
 LA English
 ED Entered STN: 3 Mar 2004
 Last Updated on STN: 3 Mar 2004
 AB Polymeric immunoglobulins (pIgs) that are present at mucosal surfaces play key roles in both the innate and adaptive immune responses. These pIgs are delivered to the mucosal surface via transcytosis across the epithelium, a process mediated by the polymeric immunoglobulin receptor (pIgR). Previous studies demonstrate that expression of the pIgR is regulated by multiple immunomodulatory factors including interleukin-4 (IL-4) and interferon-gamma (IFN-gamma). In studies using human intestinal epithelial cells (HT29), multiple inhibitors of the transcription factor nuclear factor-kappaB (NF-kappaB), including a dominant negative IkappaBalpha-serine mutant, inhibited both IL-4- and IFN-dependent increases in pIgR expression. Under identical conditions, NF-kappaB inhibitors had no effect on cytokine-dependent increases in expression of the transcription factor interferon regulatory factor-1. Over-expression of the IkappaBalpha-serine mutant also inhibited reporter gene expression in response to IL-4, TNF-alpha, IL-1beta, and in some cases IFN-gamma using constructs with sequences from the pIgR promoter. Reduced levels of pIgR were observed even when inhibitors were added 24 hr after cytokines suggesting that prolonged activation of NF-kappaB is required. Finally, reporter gene studies with NF-kappaB enhancer elements indicated that IFN-gamma alone and IL-4 in combination with other cytokines activated NF-kappaB in HT29 cells. Together, these studies provide additional insight into the signalling pathways that contribute to expression of the pIgR, a critical player in mucosal

immunity.

L32 ANSWER 13 OF 13 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

AN ~~1994:499687~~ BIOSIS

DN ~~PREV199497512687~~

TI Alternatively spliced, germline J-alpha-11-2-C-alpha mRNAs are the predominant T cell receptor alpha transcripts in mouse kidney.

AU Madrenas, Joaquin; Vincent, Dianne H.; Kriangkum, Jitra; Elliott, John F.; Halloran, Philip F. [Reprint author]

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SO Molecular Immunology, (1994) Vol. 31, No. 13, pp. 993-1004.
CODEN: MOIMD5. ISSN: 0161-5890.

DT Article

LA English

ED Entered STN: 28 Nov 1994

Last Updated on STN: 28 Nov 1994

AB We recently reported the expression of a truncated T cell receptor (TCR) alpha mRNA in kidney and brain of normal mice. In the kidney, the truncated TCR alpha transcript was expressed by bone marrow-dependent, non-T large interstitial cells located predominantly in the medulla. Here, we report the molecular characterization of the truncated TCR alpha transcript from kidney. Using a modified anchored-PCR (A-PCR) technique and directional cloning, 37 cDNA clones extending 5' of the C alpha region were generated. cDNA sequencing showed that 29 of the clones (78%) originated in the J-alpha 11-2 region. Of these clones, 17 started upstream or in the J-alpha 11-2 exon and contained the entire J-alpha 11-2 sequence correctly spliced to the first C-alpha exon. Analysis of the sequence revealed the presence of multiple stop codons in all three reading frames. The other 12 clones originated further upstream of the J-alpha 11-2 exon and did not include the J-alpha 11-2 exon, but rather arose from the joining of a cryptic splice donor signal to the usual TCR alpha C splice acceptor. This alternatively spliced transcript contained an open reading frame extending from the upstream J-alpha 11-2 region to 82 nucleotides downstream of the beginning of the TCR C alpha region, and potentially encoded a 36 amino acid polypeptide. The remaining eight clones all contained the J-alpha TA61 region correctly spliced to C-alpha with two of these extending upstream of the J-alpha TA61 exon. The predominance of J-alpha 11-2-C-alpha containing clones was confirmed by **RNase protection assay** using total RNA from kidney and spleen of scid mice. The 3' region of the transcript contained a fully conserved, correctly spliced TCR alpha C region which was polyadenylated at the 3' end. The truncated TCR alpha mRNA could be detected in preparations of cytoplasmic RNA, indicating that this transcript follows a normal RNA processing pathway. Our results demonstrate that the truncated TCR alpha mRNA expressed in normal mouse kidney is a germline J-C transcript resulting from transcription initiated predominantly upstream of the J-alpha 11-2 region. This germline transcript in the kidney is undergoing alternative splicing leading to the appearance of an open reading frame coding for a short polypeptide. These results suggest that the product of this transcript may be functionally relevant.

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Alternatively spliced, germline J α 11-2-C α mRNAs are the predominant T cell receptor α transcripts in mouse kidney

Joaquin Madrenas^{*,†,§}, Dianne H. Vincent[†], Jitra Kriangkum[‡], John F. Elliott[‡] and Philip F. Halloran^{*,†,✉}

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Abstract

We recently reported the expression of a truncated T cell receptor (TCR) α mRNA in kidney and brain of normal mice. In the kidney, the truncated TCR α transcript was expressed by bone marrow-dependent, non-T large interstitial cells located predominantly in the medulla. Here, we report the molecular characterization of the truncated TCR α transcript from kidney. Using a modified anchored-PCR (A-PCR) technique and directional cloning, 37 cDNA clones extending 5' of the C α region were generated. cDNA sequencing showed that 29 of the clones (78%) originated in the J α 11-2 region. Of these clones, 17 started upstream or in the J α 11-2 exon and contained the entire J α 11-2 sequence correctly spliced to the first C α exon. Analysis of the sequence revealed the presence of multiple stop codons in all three reading frames. The other 12 clones originated further upstream of the J α 11-2 exon and did not include the J α 11-2 exon, but rather arose from the joining of a cryptic splice donor signal to the usual TCR α C splice acceptor. This alternatively spliced transcript contained an open reading frame extending from the upstream J α 11-2 region to 82 nucleotides downstream of the beginning of the TCR C α region, and potentially encoded a 36 amino acid polypeptide. The remaining eight

clones all contained the J α TA61 region correctly spliced to C α with two of these extending upstream of the J α TA61 exon. The predominance of J α 11-2-C α containing clones was confirmed by RNase protection assay using total RNA from kidney and spleen of scid mice. The 3' region of the transcript contained a fully conserved, correctly spliced TCR α C region which was polyadenylated at the 3' end. The truncated TCR α mRNA could be detected in preparations of cytoplasmic RNA, indicating that this transcript follows a normal RNA processing pathway. Our results demonstrate that the truncated TCR α mRNA expressed in normal mouse kidney is a germline J-C transcript resulting from transcription initiated predominantly upstream of the J α 11-2 region. This germline transcript in the kidney is undergoing alternative splicing leading to the appearance of an open reading frame coding for a short polypeptide. These results suggest that the product of this transcript may be functionally relevant.

Author Keywords: T cell receptor α genes; kidney interstitial cells; germline transcripts; splicing

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